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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/183,789	10/30/98	MARTELANGE V	L0461/7047

HM12/1025

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EXAMINER	
HARRIS, A	

ART UNIT	PAPER NUMBER
1642	14

DATE MAILED: 10/25/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/183,789	Applicant(s) Martelange et al.
	Examiner Alana M. Harris, Ph. D.	Group Art Unit 1642

☒ Responsive to communication(s) filed on *August 7, 2000.*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1, 8, 9, 18-20, 24, 28, 35, 38, 40, 41, 43, 45, 47, and 50-60* is/are pending in the applicat

Of the above, claim(s) *20, 24, 28, 35, 38, 45, and 47* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 8, 9, 18, 19, 40, 41, 43, and 50-60* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. Claim 60 has been added.

Claims 1, 9 and 42 have been amended.

Claims 1, 8, 9, 18-20, 24, 28, 35, 38, 40, 41, 43, 45, 47 and 50-60 are pending.

Claims 20, 24, 28, 35, 38, 45 and 47, drawn to non-elected inventions are withdrawn from examination.

Claims 1, 8, 9, 18, 19, 40, 41, 43, 50 and 50-60 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

3. The disclosure is objected to because of the following informality: it contains embedded hyperlinks or other forms of browser-executable code listed on page 55 that is impermissible and requires deletion (see MPEP 608.01(p)). Applicant is advised to **review the entire specification** for similar errors. Appropriate correction is required. The Examiner acknowledges the corrections made to the specification in response to the first action on the merits, Paper Number 12 (mailed May 9, 2000).

Withdrawn Rejections

4. The rejection of claims 40, 41 and 43 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicants clarification of the record.

5. The rejection of claims 1, 9, 18, 19, 50 and 59 under 35 U.S.C. 102(b) as being anticipated by Accession Number U89672 (March 21, 1997) and Rees et al. (BioTechniques 20:102-110, 1996) is withdrawn in view of Applicants' arguments.

6. The rejection of claim 9 under 35 U.S.C. 102(b) as being anticipated by Accession Number AA213817 (August 13, 1997) is withdrawn in view of Applicants' amendment to the claim.

7. The rejection of claims 1, 9, 18, 19, 50 and 59 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,464,745 (filed March 31, 1993) is withdrawn in view of Applicants' arguments.

8. The rejection of claims 41 and 57 under 35 U.S.C. 103(a) as being unpatentable over Accession #U89672 and Rees et al. is withdrawn in view of Applicants' arguments.

9. The rejection of claims 43 and 58 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent #5,434,745 is withdrawn in view of Applicants' arguments.

Maintained Rejections and New Rejections

Claim Rejections - 35 U.S.C. § 112

10. The rejection of claims 1, 8, 9, 18, 19, 51-56 and newly added claim 60 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained and made.

Applicants argue the invention was enabled by the specification as filed, the invention was also fully described at the time of filing in full, clear, concise and exact terms, thus Applicants were in possession of the claimed invention at the time of filing. Applicants state they did not claim "genes" containing the disclosed sequences, but rather the claims at issue are specifically directed to "isolated nucleic acid molecules". Applicants further state that they do not understand why the function of open reading frames is pertinent to a determination of adequate written description of nucleic acid molecules and they feel it is enough that Applicants have disclosed the sequence of open reading frames. This is not found persuasive.

Granted the Applicants did not claim "genes", they did claim nucleic acids that encode amino acid sequences, SEQ ID NO: 39 and 44. The aforementioned claims embrace DNAs that encode protein products of genes from which the cDNA clones of the instant application were

derived. One of skill could isolate many cDNA sequences but would not be able to determine if they read on the claimed invention absent further information regarding reading frame, full-length sequence and protein encoded. There is no sufficient objective evidence that the reading frame from which the predicted amino acid sequence have been derived is indeed, a correct reading frame. Given that this is not clear that the instant sequences are full length and the predicted amino acid sequence may or may not be reflective or a true, in frame and expressed protein, the specification does not provide adequate written description for the isolated DNA molecules comprising the instant sequences or for DNA molecules encoding proteins. There is no description or working example of definitive identifying characteristics of the encoded polypeptides, i.e. molecular weight, shape, membrane association defining biological activity or function or even assays which reliably and predictably detect the polypeptides or of the full length cDNA which encodes the polypeptides. The Applicants have noted that they have disclosed the sequence of open reading frames, as well as suggested to the Examiner to review pages 13-17 and 26. The specification seems to be silent in regards to the possession of the entire open reading frame supporting that the instant sequences are indeed full length and that the predicted amino acid sequence is that of a full length protein which is expressed as a sarcoma associated gene product. For the recited reasons there is no adequate written description of the nucleic acid molecules.

11. The rejection of claim 40 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

Applicants argue "It is not necessary for the Applicants to establish the roles played by sdph3.10 and sdp3.5 in the development of cancer, but rather to indicate that there is potential..., as well as there are "...possible difficulties in antisense therapies, but that these hypothetical situations do not in and of themselves preclude the use of antisense in cancer treatment". The Applicants allege that the Examiner did not consider all of the Wands factors and that "Applicants maintain that the person of skill in the art of molecular biology or medicine would know how to prepare, test and use the claimed antisense nucleic acid compositions. This is not found persuasive.

The Examiner submits to the fact that one skilled in the art could make a composition comprising an antisense nucleic acid which binds to a tumor associated nucleic acid molecule as claimed, however the Applicants have yet to prove that such a composition would be enabled. The quantity of experimentation necessary to identify such a composition would be a herculean task to accomplish, especially since as noted in the previous office action that the nucleic acid is merely associated with tumors and the specification is silent on what specific tumors could such a composition would be effective against. The amount of direction or guidance presented in the specification and the presence of working examples is not sufficient to enable a composition that

will be administered to a patient to reduce the expression of the tumor associated nucleic acid. The Applicants suggest what effect is desired of the claimed composition and methodology that considers patient parameters when administering this composition, however this *in vivo* therapeutic as read in the claims and specification is arbitrarily given to almost any animal with a tumor. There needs to be an established role designated for sdph3.10 and sdp.3.5 when the claims read on a composition geared toward treating. By nature of the claimed invention there is needs to be some examples of the effective use of the molecules as a pharmacological agent. The state of the prior art, in which for example the Examiner cited Rojanasakul stated the possible difficulties one of skill in the art must be cognizant of when employing the use of such claimed compositions. The Examiner concurs that the reference cited was dated in 1996, nevertheless more recent optimistic publications do not preclude the risks involved in antisense gene therapy. The Examiner respectfully acknowledges the Applicants' opinion, however the specification is silent on the obstacles that must be overcome to successfully utilize such a claimed composition in an *in vivo* setting. Given the level of one of ordinary skill in the art to reduce the claimed invention of making the composition is enabled, however to successfully utilize the composition is not. Randomly administering the claimed composition to one bearing a tumor, any tumor to determine the antisense would indeed be burdensome to one of relative skill in the art. Therefore, due to the unpredictability of therapeutics and the absence of any evidence concerning the effectiveness of the claimed composition as a pharmacological agent, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected,

to make and use with a reasonable expectation of success, the invention commensurate in scope with this claim. The association provides no guidance as to how the instant antisense nucleic acid can be employed as therapeutic nor a basis to predict its efficacy.

12. The rejection of claims 1, 18, 19, 41, 43, 51-58 and newly added claim 60 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained and made.

a. The recitation "...hybridize under stringent..." in claims 1 and 40 is not clear. The metes and bounds are unclear and in the absence of limitations specifying specific stringency conditions. Applicants' argue that "...the disclosure of specific sets of conditions in the specification serves to define clearly the claim term "stringent conditions" when the claims are read in combination with the specification." and "...Applicants should not be limited to these exact conditions because one of ordinary skill in the art knows of hybridization conditions...". This is not found persuasive. Applicants are reminded that the claims define the subject matter of this invention and that the specification cannot be relied upon to read limitations into the claims. As written the claims allow nucleic acid molecules that differ from the nucleic acid molecules of claim 1(a) in codon sequence due to the degeneracy of the genetic code to hybridize.

b. The recitation "sarcoma associated gene product" in claims 1 and 60 are vague and indefinite. What is deemed a "sarcoma associated gene product"? Is it a polypeptide with some

sequence homology to a "sarcoma gene product"? What properties must this gene product have to be associated? Accordingly, the metes and bounds are unclear.

c. The recitations "tumor associated nucleic acid" and "tumor associated polypeptide" in claims 40, 41, 43 and 50 are vague and indefinite. What properties must these nucleic acids and polypeptides possess in order to be just associated with tumors? Do these terms mean they are not clearly tumor nucleic acids nor tumor polypeptides? Accordingly, the metes and bounds are not clear.

d. Claims 9, 57 and 58 are vague and indefinite in the recitation "...at least a portion...". The Applicants argue that the definition recited in Random House Webster's Dictionary is common and accepted and should delineate the meaning of the word. The Applicants also note that the word "portion" encompasses all possible lengths of the designated nucleic acid that are smaller than the designated nucleic acid and larger than an amplified product of two nonoverlapping 12-32 primers as claimed. This is not found persuasive. The Examiner concurs with the definition as presented by Webster, however where on the record is Applicants' meaning of "portion" found in the disclosure? Accordingly, the metes and bounds are unclear. To obviate this rejection Applicants are requested to further clarify their meaning of the word "portion".

Claim Rejections - 35 U.S.C. § 101

13. The rejection of claims 1, 8, 9, 18, 19 and 51-56 and newly added claim 60 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility, or a well established utility is maintained and made.

Applicants' argue that they have provided well-established utilities and point out in the specification several instances that allegedly provide support for these claimed utilities. The Applicants state that the Examiner has not presented arguments as to why all of the asserted utilities are not believable. These arguments are not found persuasive.

The Examiner has carefully considered Applicants' arguments and agree with Applicants that the utility is indeed credible, but not specific or substantial. The question still remains how can one skilled in the art utilize the claimed nucleic acid molecules and polypeptides in the diagnosis and treatment of conditions that are not tissue specific? As observed in Table III, page 50 of the specification sdph 3.10 is expressed in several tumor types in different organs. Surely one skilled in the art would recognize that the claimed nucleic acids and their encoded polypeptides can not be employed as discriminate tumor marker when their expression is not discriminate. Likewise, could these claimed molecules be totally useful in detection assays when they are only indifferently described as tumor associated? Consequently there is know information that links expression of the resulting **merely** tumor **associated** polypeptides to any specific tissue. Thus, the asserted utility of the claimed nucleic acids is not substantial or specific.

Claims 1, 8, 9, 18, 19, 51-56 and 60 are also rejected under 35 U.S.C., first paragraph. Specifically, since the claimed invention is not supported by either and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 U.S.C. § 102

14. Claims 1, 18, 19, 50 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Accession Number AA213817 (August 13, 1997) is maintained. The Applicant's argue that Accession #AA213817 is an EST from a germinal center B cell tumor. This is not found persuasive. As written this nucleic acid from the recited accession reads on the claim. This is indeed an isolated nucleic acid molecule capable of hybridizing under stringent conditions to a nucleic acid of SEQ ID NO:43.

15. Claims 1, 9, 18, 19, 50 and 59 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,880,102 (filed Jan. 17, 1995). Applicant's argue that "an unknown vector for the '102 patent, as SEQ ID NO:1 is not described in the patent and does not apparently match any of the lengths of sequences in the Figures of the '102 patent. This is not found persuasive. The match between Applicants' SEQ ID NO:38 and '102's SEQ ID NO:1 can be found on the nucleic acid database sheet sent to Applicants within Paper #12, mailed May 9, 2000, as well as in patent '102, columns 15 and 16 starting at base #995-1034. These bases match #21-60 of

Applicants' SEQ ID NO:38. There is not evidence within the recited patent that these nucleic acids from '102 are vector sequences and do not code for a sarcoma associated gene product.

16. Claim 60 is rejected under 35 U.S.C. 102(b) as being anticipated by Accession Number W86797 (July 1, 1996). Accession #W86797 discloses an isolated nucleic acid molecule selected from the group consisting of:

(a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence set forth as SEQ ID NO:1, which codes for a sarcoma associated gene product,

(b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code,

(d) complements of (a) and (b).

Claim Rejections - 35 U.S.C. § 103

17. The rejection of claims 41 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent #5,880,102 is maintained. Applicants' argue that the recited reference does not teach the limitations of the claimed invention. This is not found persuasive for the reasons listed in paragraph # 15 and in Paper 12, paragraph 17.

18. The rejection of claims 43 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Accession #AA213817 is maintained for the reasons set forth in paragraph #14 and Paper #12, paragraph #18.

19. Claims 8, 40 and 51-56 are free of the art.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris whose telephone number is (703) 306-5880. The examiner can normally be reached on Monday through Friday from 7:00 am to 3:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Alana M. Harris, Ph.D.
Patent Examiner, Group 1642
October 23, 2000

Sheela J. Huff

SHEELA HUFF
PRIMARY EXAMINER